

## **2.0 DESCRIPTION OF PROPOSED RESEARCH IN NON-TECHNICAL LANGUAGE**

Cystic fibrosis (CF), the most common inherited disease in North America, is caused by problems in a gene known as "CFTR". Normal functioning of this gene is required for the movement of water and salt across airway cells. Persons with this disease have abnormal mucous in their lungs which builds up over time and leads gradually, over many years, to serious lung disease. Attempts are being made to replace the missing gene function using special gene carriers, or vectors, which carry corrected genes into cells. The types of vectors tested in patients so far have a temporary effect and therefore may not be ideal for treating CF lung disease. Targeted Genetics Corporation has developed a different type of vector, called tgAAVCF, which is based on a virus, AAV. Many people have been infected by the naturally occurring type of AAV without realizing it, as AAV does not cause disease. AAV is able to maintain its DNA for long periods of time in the cells that it enters. This vector may slow or stop lung destruction seen in cystic fibrosis patients. Our tests of AAV vectors carrying the CFTR gene have shown it to be biologically active in cells in the test tube and in animals. This vector has been given to 45 patients without serious side effects.

One of the many complications of CF is ongoing lung infection, inflammation and destruction. The study described herein proposes to administer tgAAVCF in a microscopic mist to the lungs of patients with CF to see if widespread delivery of this vector to the entire lung is safe. Measurements will be taken to determine whether the vector is present and active in the lung. Cystic fibrosis patients, greater than 15 years of age, will initially undergo a bronchoscopy to collect baseline information prior to gene therapy treatment. Patients will be seated in a clear, vinyl isolation chamber, similar to an oxygen tent, and will receive tgAAVCF into their lung by inhalation of mist. Patients will inhale and exhale through a mouthpiece, with a nasal clip used to ensure that vector is not exhaled through the nose. Additional bronchoscopies will be performed to measure vector activity in the lung. Results from this trial will be used to design future studies which will attempt to actually treat or prevent lung deterioration with CF.